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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,219	09/08/2003	Bruce Joseph Roser	559662000102	2707
25225	7590	03/21/2006	EXAMINER	
MORRISON & FOERSTER LLP 12531 HIGH BLUFF DRIVE SUITE 100 SAN DIEGO, CA 92130-2040			PRATS, FRANCISCO CHANDLER	
			ART UNIT	PAPER NUMBER
			1651	

DATE MAILED: 03/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/658,219

Applicant(s)

ROSER, BRUCE JOSEPH

Examiner

Francisco C. Prats

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20-33 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 20-33 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 12-19-03.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: ____.

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DETAILED ACTION

The preliminary amendment filed February 21, 2006, has been received and entered.

Claims 20-33 are pending and are examined on the merits.

Claim Rejections - 35 USC § 112

Claims 31-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, claim 31 recites "reconstituting the composition of claim 20." However, claim 20 does not recite a composition. Rather, claim 20 recites a vial which contains a composition. It is unclear how the vial can be reconstituted to prepare a therapeutic injectable preparation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been

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obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 20-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curtis et al (U.S. Pat 5,824,780) in view of Livesey et al (U.S. Pat. 5,364,756) and Lee et al (EP 0 314 095).

Curtis describes a process of producing an activated and stabilized Factor VIII in the absence of albumin. See claim 1, at column 9. The Factor VIII is clearly separated from albumin, as evidenced by the removal of "other proteins" from the Factor VIII preparation. See step (b) of claim 1, at column 9, line 46 through column 10, line 3. The Factor VIII is stabilized by the addition of a stabilizing additive which may be trehalose. See claim 4, at column 10. Note the recitation of trehalose and albumin as *alternative* stabilizing additives. Curtis also describes that after preparation of the stabilized solution of Factor VIII, the Factor VIII is lyophilized. See claim 5, at column 10.

See also, the discussion at col. 5, lines 30-43, stating that "[e]xamples of stabilizers include albumin ... and trehalose", and that "[f]ollowing preparation and stabilization of the activated Factor VIII, the protein can be lyophilized and

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stored at reduced temperatures" Col. 5, lines 4-6. Note that Curtis lists recombinant Factor VIII as being suitable for use in the disclosed process. Column 2, lines 61, et seq. Thus, taken as a whole, Curtis clearly describes a process wherein an aqueous solution of Factor VIII in the absence of albumin is lyophilized in the presence of trehalose, are cited in the claims.

Curtis differs from the claims under examination by failing to describe the lyophilization of native Factor VIII. However, Livesey clearly provides motivation for lyophilizing "native" Factor VIII in trehalose without albumin by not only claiming a specific embodiment (claim 17) of lyophilizing Factor VIII, but also disclosing that trehalose, and not albumin, is one of a number of agents particularly suited to dry preservation of macromolecules such as proteins. See col. 9, lines 16 -32:

For example, trehalose and polyhydroxyl carbohydrates bind to and stabilize macromolecules such as proteins and nucleic acids in a virus or vaccine sample when dried, thereby protecting the integrity of the sample. Various dry protectants can be used in the present invention: sucrose, raffinose, trehalose, zinc, proline (or other protein stabilizers), myristic acid (a known thermostabilizer of vaccines), spermine (a polyanionic compound) and combinations thereof.

Thus, the artisan of ordinary skill seeking to preserve the "native" Factor VIII encompassed by Livesey's claim 17, recognizing that Factor VIII is a protein, clearly would have

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looked to trehalose instead of albumin, based on Livesey's disclosure that trehalose is one of a number of agents particularly suited for protein protection in freeze-drying procedures, and albumin is not. Additional motivation for freeze-drying Factor VIII using trehalose in the absence of albumin would have been derived from the fact that the lone example of protein freeze-drying of Livesey, Example 5 at columns 23 and 24, demonstrates that the integrity of a protein-containing viral vaccine is adequately protected by trehalose in buffer with no other preservative agents, and that the vaccine produced thereby is stable at room temperature for two weeks, in vials, as recited in the claims under examination.

While Livesey discloses the presence of calcium ion in one of the potential buffer solutions (see, e.g., claim 7, at column 25, line 10), neither Livesey nor Curtis explicitly disclose the presence of calcium ion in a native Factor VIII preparation. However, Lee et al clearly discloses the desirability of using the claimed amount of calcium chloride in buffers for use in lyophilizing factor VIII. See, e.g., claims 1-3 at lines 12-21 of page 8. Thus, applicant's selection of a concentration of calcium known to be useful in the preservation of factor VIII clearly would have been obvious at the time of applicant's invention.

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Regarding the claimed amount of trehalose, one of ordinary skill practicing the preservation techniques of Curtis or Livesey clearly would have recognized that the ratio of trehalose preservative agent to Factor VIII would have affected the result of the preservation process. Thus, the determination of a suitable amount of trehalose, including that claimed, would have been a matter of routine optimization of a result-effective parameter on the part of the artisan of ordinary skill, and therefore clearly obvious under 35 U.S.C. § 103(a).

Lastly, regarding the reconstitution of the dried materials in saline or water, note specifically that at the time of applicant's invention it was well known that both of these vehicles was suitable for injection, the known method of administration of Factor VIII. A holding of obviousness is therefore required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re*

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Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 20-33 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of U.S. Patent No. 6,649,386, in view of Livesey et al (U.S. Pat. 5,364,756) and Lee et al (EP 0 314 095). Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims recite the preparation of a composition as recited in the claims under examination herein, and useful in the preparative methods recited in the claims under examination, except that the patented claims do not recite the presence of calcium in the dried product. However, as discussed above, Livesey discloses the desirability of placing the Factor VIII preparations in vials such that they are storage stable without refrigeration, and Lee disclose the desirability of including calcium ion in

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preparations of the type recited in the patented claims. One of ordinary skill would therefore have been motivated to have placed the product resulting from the patented process in a storage-stable vial, and to have added the amount of calcium recited in the claims under examination to the compositions resulting from the patented claims. Moreover, as discussed above regarding the amount of trehalose recited in the claims under examination, one of ordinary skill practicing the preservation techniques of Curtis or Livesey clearly would have recognized that the ratio of trehalose preservative agent to Factor VIII would have affected the result of the preservation process. Thus, the determination of a suitable amount of trehalose, including that claimed, would have been a matter of routine optimization of a result-effective parameter on the part of the artisan of ordinary skill, and therefore clearly obvious.

A terminal disclaimer is clearly required.

Claims 20-33 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of copending Application No. 10/679,723 in view of Livesey et al (U.S. Pat. 5,364,756) and Lee et al (EP 0 314 095). The claims under examination and the claims of the copending application differ in that the claims

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under examination herein recite that the composition is in a vial. However, as discussed above, Livesey makes it clear that the lyophilized preparation disclosed therein were suitable for placement in vials and storage at room temperature. Thus, one of ordinary skill clearly would have been motivated to have placed the composition recited in the copending claims in a vial in the manner recited in the claims under examination herein. The claimed composition is therefore properly considered obvious over the vial-contained composition of the copending application. Lee demonstrates the obviousness of the claimed amount of calcium.

This is a provisional obviousness-type double patenting rejection.

Claims 20-33 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of copending Application No. 09/888,734 in view of Livesey et al (U.S. Pat. 5,364,756) and Lee et al (EP 0 314 095).

The claims under examination differ from the copending claims in that the copending claims recite the preparation of a composition as recited in the claims under examination herein, and useful in the preparative methods recited in the claims

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under examination, except that the copending claims do not recite the presence of calcium in the dried product. Livesey discloses the desirability of placing the Factor VIII preparations in vials such that they are storage stable without refrigeration, and Lee disclose the desirability of including calcium ion in preparations of the type recited in the patented claims. One of ordinary skill would therefore have been motivated to have placed the product resulting from the process recited in the copending claims in a storage-stable vial, and to have added the amount of calcium recited in the claims under examination to the compositions resulting from the patented claims. Moreover, as discussed above regarding the amount of trehalose recited in the claims under examination, one of ordinary skill practicing the preservation techniques of Curtis or Livesey clearly would have recognized that the ratio of trehalose preservative agent to Factor VIII would have affected the result of the preservation process. Thus, the determination of a suitable amount of trehalose, including that claimed, would have been a matter of routine optimization of a result-effective parameter on the part of the artisan of ordinary skill, and therefore clearly obvious.

This is a provisional obviousness-type double patenting rejection.

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Claims 20-33 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of copending Application No. 10/681,948 in view of Lee et al (EP 0 314 095).

Although they do not recite identical embodiments, the claims of the copending application recite Factor VIII compositions comprising the same amounts of calcium and trehalose as in the claims under examination herein. While the copending claims recite the presence of histidine in certain embodiments, Lee clearly discloses the desirability of adding histidine to cryopreserved Factor VIII compositions. See, e.g., claims 1-3, at page 8, lines 12-21.

Moreover, as discussed above, Livesey discloses the desirability of placing the Factor VIII preparations in vials such that they are storage stable without refrigeration, and Lee disclose the desirability of including calcium ion in preparations of the type recited in the patented claims. One of ordinary skill would therefore have been motivated to have placed the product recited in the copending claims in a storage-stable vial, and to have added the amount of calcium recited in the claims under examination to the compositions resulting from the patented claims. Moreover, as discussed above regarding the

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amount of trehalose recited in the claims under examination, one of ordinary skill practicing the preservation techniques of Curtis or Livesey clearly would have recognized that the ratio of trehalose preservative agent to Factor VIII would have affected the result of the preservation process. Thus, the determination of a suitable amount of trehalose, including that claimed, would have been a matter of routine optimization of a result-effective parameter on the part of the artisan of ordinary skill, and therefore clearly obvious.

This is a provisional obviousness-type double patenting rejection.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C. Prats whose telephone number is 571-272-0921. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the

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organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Francisco C. Prats
Primary Examiner
Art Unit 1651

FCP